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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
AULAKH, CHARANJIT	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,070	ANDERSSON ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-14,17,18 and 20-35* is/are rejected.

7)☒ Claim(s) *15,16 and 19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. According to paper filed on Oct. 12, 2004, the applicants have elected group II (m is 1) without traverse for further prosecution. The applicants have also amended claims to delete non-elected subject matter and furthermore, have canceled claim 8.

2. Claims 1-7 and 9-35 are now pending in the application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 and 25-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating psychosis using instant compounds of formula I or a pharmaceutically acceptable salt, does not reasonably provide enablement for inhibiting activity of monoamine receptor, inhibiting activation of monoamine receptor, treating a disease condition associated with a monoamine receptor or treating psychosis using amide, ester or prodrug of compounds of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed: Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the

prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, the state of prior art, presence of working examples and the breadth of claims.

The instant compounds are inverse agonists at 5-HT2A receptors as taught by the instant specification and therefore, will have utility in treating psychosis. The instant specification teaches that existing antipsychotic drugs interact with a large number of monoamine receptors such as dopaminergic, serotonergic, adrenergic, muscarinic, histaminergic etc. (see page 3, third paragraph) and further teaches that the therapeutic and adverse effects of these drugs are mediated by distinct receptor subtypes. The specification further teaches that there is a need to develop drugs that are selective for individual receptor classes and subclasses among monoaminergic receptors. The specification also teaches that there are atleast 15 genetically distinct 5-HT receptor subtypes, each subtype display a unique distribution, preference for various ligands, and functional correlate(s) (see page 2, middle paragraph). As stated earlier, serotonin is one of the several other known monoamines present in the central nervous system and furthermore, each of these monoamines have numerous receptor subtypes. There is no teaching either in the specification or prior art that the instant compounds or closely related compounds in the prior art will act as an agonists or antagonists at each of the 15 known 5-HT receptor subtypes or numerous receptor subtypes of all known monoaminergic receptors such as dopaminergic, adrenergic, cholinergic, histaminergic

etc. The utility of the instant compounds will depend upon agonist versus antagonist activity at each of these various monoaminergic receptor subtypes. There is no teaching in the specification regarding association of any disease condition with either hyperactivity or hypoactivity of any monoamine receptor subtype. There are no working examples present to show efficacy of instant compounds in known animal models of any disease condition associated with any monoamine receptor subtype. There is no guidance or direction provided how the instant compounds having inverse agonist activity at 5-HT2A receptors will have utility in treating disease conditions associated with all other serotonin receptor subtypes or all known monoamine receptor subtypes. There is not even a single example of an amide, ester or prodrug of the instant compounds of formula I present in the specification. The instant compounds of formula I encompasses hundreds of thousands of compounds based on the values of variables R1, R2, R3, Ar1, Ar2, X, W and n and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate the efficacy of instant compounds in known animal models of every possible disease condition associated with all known monoamine receptor sybtypes and hence their utility for treating these disease conditions.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 14 and 24-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the terms---amide, ester or prodrug---- are indefinite since specific amides, esters or prodrugs are not defined and furthermore, it is not clear whether they will also retain activity as inverse agonist at 5-HT2A receptors.

In claim 1, the value of variables R2 and R3 defined as ---forms a ring---is indefinite since the size of the ring, degree of saturation, number and type of heteroatoms present are not defined.

Claim 14 recites the limitation "alkyl or alkoxy" in claim 12. There is insufficient antecedent basis for this limitation in the claim.

Claim 24 contains several compounds which do not read upon the elected group (compounds of formula I) such as 5th compound on page 6, first three compounds on page 7, second compound on page 9 and third compound from bottom on page 11.

In claims 25-35, the terms ---monoamine receptor and diseases associated with monoamine receptors ----- are indefinite since specific receptor subtypes and disease conditions associated with these specific receptor subtypes are not defined.

Claim Rejections - 35 USC § 102

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-7, 9-14, 17, 18 and 20-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Anderson (U.S. Patent 6,756,393).

Anderson discloses Azacyclic compounds having inverse agonist activity at 5-HT2A receptor subtype for treating psychosis. The compound disclosed in column 18 (see

lines 28-29) by Anderson anticipates the instant claims when both Ar1 and Ar2 represent substituted phenyl group, X is methylene, W is O and R1 represents heterocyclyl-alkyl group in the instant compounds of formula I.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

8. Claims 1-3, 5-12, 14, 17 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Leach (WO 03/086400).

Leach discloses n-substituted pyridinone and pyrimidinone derivatives for treating Artherosclerosis. The exemplified compounds 12 and 13 (see page 27) disclosed by Leach anticipate the instant claims when Ar2 represents heteroaryl group, Ar1 represents an aryl group, X is methylene, W is O and R1 represents heterocyclyl-alkyl group in the instant compounds of formula I.

Allowable Subject Matter

9. Claims 15, 16 and 19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is

(571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625